Site visit inspection report on compliance with HTA licensing standards

Unilever Research and Development Port Sunlight

HTA licensing number 12074

Licensed under the Human Tissue Act 2004 for the

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

5 & 6 March 2019

Summary of inspection findings

The HTA found the Designated Individual (DI), the Licence Holder (LH), the premises and the practices to be suitable in accordance with the requirements of the legislation.

Although the HTA found that Unilever Research and Development Port Sunlight had met the majority of the HTA's standards, six major and nine minor shortfalls were found against a range of standards across the four main standards groups.

The DI has also been given advice on a range of issues and particular examples of strengths and good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. They are grouped under four headings:

- consent
- governance and quality systems
- traceability
- premises facilities and equipment.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is provided.

HTA inspection reports are published on the HTA's website.

Background to the establishment

This report refers to activities carried out by Unilever Research and Development Port Sunlight ('the establishment' and 'hub site') at the Port Sunlight site in Wirral and the associated satellite site at the University of Liverpool, Materials Innovation Factory (MIF) site in Liverpool.

The Designated Individual (DI) is the Safety, Quality and Environment (SQE) Manager, based at the hub site, and also sits on the Unilever Ethics Committee. The Corporate Licence Holder (CLH) is Unilever Central Resources UK and the Corporate Licence Holder contact (CLHc) is the Site Leader of the Unilever Port Sunlight site.

In June 2007, the establishment was granted a licence in the HTA's research sector for the 'storage of relevant material for use for a scheduled purpose', which in this case is, 'Research in connection with disorders, or the functioning, of the human body'. There have been no changes to the DI since the licence was granted; however, there have been some changes to the Persons Designated (PDs) and CLHc on the licence since it was granted.

The establishment is one of many Unilever sites across the world and is part of a major global company, supplying leading brands in personal care, household care, foods & refreshments. Unilever Port Sunlight and the Materials Innovation Factory, University of Liverpool site house several functions of Unilever's research and development groups.

Within Unilever Research and Development Port Sunlight, there are three distinct functions, including Home Care, Central Functions and Beauty and Personal Care / Science and Technology (B&PC/ST). Only one of these Unilever groups operates under this particular HTA licence: this group uses human tissue for various different projects to assist with the innovation and development of hair, oral care and deodorant/anti-perspirant products. Recently, Unilever R&D Global went through an organisational restructure, which resulted in the merger of Beauty and Personal Care and Science and Technology, previously two separate functions. The B&PC / ST group uses human tissue for various different projects to assist with the innovation and development of hair, oral, deodorant and household products. Human tissue is either retrieved from healthy volunteers, third party suppliers or is a waste product of cosmetic surgery that has been consented for research from a third party supplier; however, no documented agreements with third parties were seen at the time of the inspection(see *shortfall against C1(c)).* Relevant material, such as human hair follicles, skin, teeth, buffer scrubs and various oral secretions are stored at either the hub or the satellite site.

The functionality of both the hub and satellite site varies depending on the project being conducted; however, all projects assist with the development of the Unilever brand. As well as consented individuals and third party suppliers, Unilever also work with Clinical Research Organisations (CROs) to assist with other research projects; however no documented agreements with CROs were seen during the inspection (see *shortfall T1(g))*. Relevant material may also be stored in future for projects covered by recognised NHS REC approvals (see *Advice item 5)*.

The establishment has different storage conditions across the two sites. During the time of the inspection, there was very little human tissue being stored, as many projects were yet to commence or had just been finalised; however, all storage locations for human tissue were inspected with some issues identified (see *shortfall PFE2 (c))*. There were seven fridges and freezers at the hub site, and two at the satellite site, these consisted of -80ºC freezers, -20ºC freezers, room temperature storage, a walk in fridge and +4ºC fridges.All storage locations have a named custodian; this person is in charge of any maintenance, servicing and cleaning of the equipment which is done on an ad-hoc basis (see *shortfall PFE1 (c)).* All storage locations were monitored via external calibrated probes; however, some were not linked to an external alarm system and there was a reliance on purely local alarms. Each item of equipment has one custodian; however, not all custodians were actively monitoring storage temperatures (see *shortfall PFE2 (c)*). Access to all storage locations which contain human tissue is through the laboratory. Access to the laboratory is controlled by the lab managers, who will authorise staff after they have undergone the induction programme satisfactorily.

Description of inspection activities undertaken

The inspection was the second routine inspection of the establishment and consisted of a visual inspection, interviews with individual staff, traceability audits, document review and a roundtable discussion with establishment staff.

At the time of the inspection, human tissue was being stored for only two projects. Traceability audits were completed on three, randomly-selected buffer scrub samples across one of the projects. There were no discrepancies for the buffer scrub samples. Three, randomly-selected samples were chosen for the dental project; however, it was not possible to complete full traceability on these samples (see *shortfall T1 (c))*. Samples were selected from the -80ºC freezers and the +4ºC fridge. Where possible, labels on the samples were noted and checked against the electronic records. Copies of the project consent forms were then reviewed.

Inspection findings

The HTA found the Licence Holder, the Designated Individual and the premises to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Consent

Standard	Inspection findings	Level of shortfall
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the HTA's Codes of Practice		
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.	The standard operating procedure (SOP) titled 'Informed Consent' was found to have the following issues: • The document review date has been exceeded. • There was no reference to the HTA or HT Act. • It was not currently being followed by staff. • The example consent form in the appendix was not used. The establishment does not have a process for donors to withdraw their consent and the procedure / process that staff should follow. Due to the various projects, there were numerous consent forms; however, not all of them were satisfactory and could be considered misleading to participants. The following issues were identified with the annual consent forms: • No initial boxes against the consent clauses, which does not indicate a regulatory breach in itself but is inconsistent with agreed establishment processes. • No witnesses for consent being taken, which does not indicate a regulatory breach in itself but is inconsistent with agreed establishment processes. • Some contained misleading information in relation to participants being able to withdraw their consent when they could not. Consent is recorded 'in bulk' for some projects. This means that a single form may contain more than 30 donor signatures. It was not clear to determine the names of the participants who gave their consent, when they did so or who obtained it.	**Major**

c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.	There were no relevant agreements for any of the tissue collected and tested on behalf of Unilever or from CROs working with Unilever. A template material transfer agreement (MTA) was seen; however, this does not reference the HTA / HT Act or provide any consent assurances for the tissue taken. The document in place for the dental study does not reference the HTA or the HT Act. There is also no consent assurance from the supplier and nothing to specify that informed consent has been given by the participants.	**Major**
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent		
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.	The training presentation that is provided to staff has the following issues: • Out of date Codes of Practice are referenced. • It contains incorrect information about the requirements of the HT Act and the HTA's regulatory framework. For example, it refers to two "overarching standards". • It references Organ Donation and the Transplant Regulations, which are not relevant to the establishment. • The age stated for a child is less than 16 years old; however, this is inconsistent with the HT Act. Evidence also demonstrated that consent was previously being sought by staff before they had receiving this training.	**Major**
c) Competency is assessed and maintained.	There are no competency assessments for consent seeking and there is no maintenance of consent training. All staff were trained in February 2019. Before this date, no staff had been trained in consent seeking.	**Minor**

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process		
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.	All SOPs also need to be up to date, within their review dates and reflective of current practices, for example, the SOP for incident reporting details specific forms that are to be used; however, the process understood and explained by staff was different to the recently updated and implemented process.	**Minor**
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.	There are no regular governance meetings, where matters relating to HTA licensed activities are discussed.	**Minor**
GQ2 There is a documented system of audit		
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.	Although previous audits had identified non-conformances, there were no clear follow-up actions. See *Advice*, item 2.	**Minor**
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored		
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.	Whilst the establishment does have risk assessments, they do not cover all of the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. *See Advice,* item *4.*	**Minor**

Traceability

Standard	Inspection findings	Level of shortfall
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail		
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.	One of the two human tissue projects had several issues in relation to the identification system used: • Some samples are pooled together to form batches and are labelled with a "Batch ID"; however, this did not relate to any documentation or coding system. The pooling of sample also meant that it was not possible to trace individual donations back to any paperwork or consent forms. In addition, the total number of donated samples within a batch is also not recorded. • Some samples were not labelled. • A small selection of samples within a collection had barcodes put on them; however this was not relatable to a tracking system and was also inconsistent with all other samples within the collection that did not have barcodes.	**Major**
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.	The lack of register for one of the projects meant that an audit trail was not maintained. During the audit, it was not possible to determine when all of the tissue was received or the consent obtained. There was a transfer log; however, this had limited information and was unclear to follow for anyone aside from the lead investigator. Due to all tissue being pooled in batches when received by the establishment, the following issues were found with the dental study; • There is no paperwork, consent forms or logs for any of the batches. • It was not possible to determine what study each tissue was being used for, disposed of or transported elsewhere. • There is also no log of how many teeth are contained within the pots.	**Major**

d) A system is in place to ensure that traceability of relevant material is maintained during transport.	The establishment did not have any system or transfer logs /location logs for tissue sent internally or externally. The establishment had agreements in place with couriers to transfer material internally; however, this did not ensure that enough details were recorded to maintain sample, for example: • what tissue was sent • how many samples • who sent them • time and date of when they were sent • when they were received • in the case of internal transfer, where they were then stored upon receipt.	**Minor**
g) Records of any agreements with recipients of relevant material are kept.	No relevant agreements were seen.	**Minor**
T2 Bodies and human tissue are disposed of in an appropriate manner		
b) The date, reason for disposal and the method used are documented.	In both of the projects, disposal is recorded but there is inconsistency; for example, some stated “destroyed” whilst others stated “disposed”. There was also no consistency in disposal records across the projects for the following areas: • the method for disposal • the unique IDs/codes for the sample being disposed of • the date of disposal • who sent the sample for disposal • reason the sample was disposed of.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are secure and fit for purpose		
c) There are documented cleaning and decontamination procedures.	The establishment does not have documented procedures for cleaning or decontamination.	**Minor**
PFE2 There are appropriate facilities for the storage of bodies and human tissue		
c) Storage conditions are monitored, recorded and acted on when required.	The following issues were found with the storage locations; • Not all of the locations were on an external alarm call out system, only internal audible alarm systems; however, no risk assessment has been undertaken in relation to this. • Some temperature logs were printed but there did not appear to be any process for the review of temperature data. There were no clear procedures for acting on excursions or fluctuations in temperature. • In some cases, only one person is a contact for the call out system. There is no alternative contact should this person be unavailable. • Whilst each storage location is assigned a custodian, there is only ever one person assigned to the location. Should this person be unavailable - for example, due to sickness or annual leave - there would be no back up to ensure that the custodian's duties are covered. • The establishment does not 'challenge test' their external call out system and therefore cannot be certain that the system works as specified.	**Major**

Advice

The HTA advises the DI to consider the following to further improve practices:

No.	Standard	Advice
1.	C1 (d)	The DI is advised to ensure that the consent information given to participants is clear and reflects the practices that are followed. For example, where a participant is unable to withdraw consent due to the pooling of their sample, ensure that this is communicated to the participant and that withdrawal is only possible prior to giving the sample or immediately after. The DI is also advised to ensure that the language used is clear and easy for the participants to understand.
2.	GQ2 (a)	The DI is advised to ensure that frequent audits are being done within a 12 month period and that the audit schedule specifies exactly when audits are due. The DI is also advised to develop the audit schedule to include more robust audits that cover a broader range of activities; for example, process audits and the referenced mock 'HTA' audits. The "HTA Audit Challenge" that is outlined in the HTA Compliance presentation could be an effective and useful tool.
3.	GQ3 (a)	The HTA Compliance presentation developed and provided by the DI is very thorough and well structured. The DI is advised, however, to ensure that consent training is specified as being a mandatory training course for those who seek consent, rather than it being optional.
4.	GQ6 (a)	The DI is advised that risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities, including: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for useful research; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment ; • security arrangements; • Incorrect disposal.
5.	T1 (b)	The DI is advised to ensure that they are fully aware of all recognised REC-approved studies / projects and that there is a suitable system to track the approval dates, expiration dates and tissue stored under the REC approval.
6.	T1 (b)	The DI is advised to ensure that staff are completing registers of all relevant human tissue samples, which should at least include their locations, the number of samples stored and types of sample. The DI is also advised to ensure that this is regularly audited by establishment staff and included in the audit schedule.

7.	PFE2 (d)	The DI is advised to strengthen the contingency plan so that staff are clear of the procude and ensure that the plan includes all of the potential issues that may arise not just the failure of the piece of equipment, for example, power loss to the equipment, power loss to the entire site or building issues such as floods.
8.	PFE3 (a)	The DI is advised to put a SOP in place for the maintenance of all storage locations. This should include the acceptable temperature ranges and the custodians for each piece of storage equipment.

Concluding comments

Although the findings of the inspection revealed several areas for improvement, and that the DI needs to have a better oversight of all activities taking place under the licence, a number of strengths and areas of good practice were observed during the inspection including:

- The establishment has robust lone working arrangements, using a combination of badge boards and tilt alarms. These alarms are also checked by security weekly, to ensure that they are both working properly.

- The establishment has maps and orientation aids throughout both the hub and satellite site.

- All staff are required to go through an extensive induction process prior to being given access to the laboratories, which includes human tissue training and assessments of competence.

The HTA found the Designated Individual (DI), the Licence Holder (LH), the premises and practices to be suitable in accordance with the requirements of the legislation.

Although the HTA found that Unilever Port Sunlight (the establishment) had met the majority of the HTA's standards, six major shortfall and nine minor shortfalls were found against a range of standards across the four main standards groups.

The HTA requires the Designated Individual to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 09 April 2019

Report returned from DI: 17 April 2019

Final report issued: 20 June 2019

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 26 November 2019

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
e) Language translations are available when appropriate.
f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
b) Records demonstrate up-to-date staff training.
c) Competency is assessed and maintained.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.
b) There is a document control system.
c) There are change control mechanisms for the implementation of new operational procedures.
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.
e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities.
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training.
b) There are documented induction training programmes for new staff.
c) Training provisions include those for visiting staff.
d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.
b) Risk assessments are reviewed regularly.
c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.
c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity.
b) Where relevant, storage arrangements ensure the dignity of the deceased.
c) Storage conditions are monitored, recorded and acted on when required.
d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
c) Staff are provided with suitable personal protective equipment.

Appendix 2: Classification of the level of shortfall

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. Critical shortfall:

A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions

or

A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

A critical shortfall may result in one or more of the following:

(1) A notice of proposal being issued to revoke the licence

(2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

(3) A notice of suspension of licensable activities

(4) Additional conditions being proposed

(5) Directions being issued requiring specific action to be taken straightaway

2. Major shortfall:

A non-critical shortfall that:

- poses a risk to human safety and/or dignity, or
- indicates a failure to carry out satisfactory procedures, or
- indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines, or
- has the potential to become a critical shortfall unless addressed

or

A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. Minor shortfall:

A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards.

This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based or site visit.

In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.